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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

AFREMOVA, VERA

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 09/09/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/024,043

Applicant(s)

BURGESS ET AL.

Examiner

Vera Afremova

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-104 is/are pending in the application.
- 4a) Of the above claim(s) 1,4,5,15-26,29-38,42-48,54-80,89-104 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 2,3,6-14,27,28,39-41,49-53 and 81-88 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,8,10,12
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Elections/Restrictions and Status of claims

Claims 1, 4, 54-63, 76-78, 89, 92- 101, 103 and 104 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to the nonelected inventions of Groups I and III-VII as explained in the prior office actions. The restriction requirement is hereby made FINAL. Applicant timely traversed the restriction requirement in Paper No. 7 filed 6/10/2003.

Applicants' election of the species with traverse in Paper No. 11 filed 6/10/2003 in response to the species election requirement with respect to the elected invention of the Group II (claims 2, 3, 5-53, 64-75, 79-88, 90, 91 and 102) is acknowledged. Applicants argue the search of the "elected species" would necessarily involve an overlapping search of the "non-elected" "species". However this is not found persuasive because as to the question of burden of search, classification or designation of elected "species" is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different "species" having materially different issues also exists. Clearly different searches and issues are involved with each "species".

The elected "species" [Paper No. 11 filed 6/10/2003] are following:

- 1) stabilizing process " c) " which is drawn to reducing temperature, and
- 2) irradiation by gamma radiation.

Claims 49-53 and 81 are directed to the elected "species" 1) which is the stabilizing process by reducing temperature. Claims 39-41 are directed to the elected "species" 2) which is irradiation by gamma radiation. Claims 2, 3, 6-14, 27, 28 and 82-88 are generic.

Therefore, claims 2, 3, 6-14, 27, 28, 39-41, 49-53 and 81-88, which are directed to the elected "species", have been examined in the instant office action and found non-patentable as explained below. Thus, claims 5, 15-26, 29-38, 42-48, 64-75, 79, 80, 90, 91 and 102 have been withdrawn from consideration as being drawn to nonelected "species".

Information Disclosure Statement

The information disclosure statement filed 4/05/2002 [Paper # 4] fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Please, provide copies at least of all non-patent literature publications.

The information disclosure statements filed on 8/26/2002 [Paper # 5], on 2/27/2003 [Paper # 8], on 4/02/2003 [Paper # 10] and on 6/13/2003 [Paper #12] have been considered.

Claim Rejections - 35 USC § 112

Claims 49 and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 49 and 53 lack antecedent basis in the method of claims 2 and 3. The method of claims 2 and 3 requires an active step of "reducing" temperature. However, claim 49 encompasses the use of the same or stable "ambient" temperature in the method for sterilization. Claim 53 encompasses increasing temperature "above ambient" in the method for sterilization. Therefore, the meaning of the limitations of claims 49 and 53 lacks antecedent basis in claims 2 and/or 3.

According to the applicants' definitions (page 27) temperature "above ambient" is above 37°C, temperature "below ambient" is below 0°C but there is no clearly defined range for "ambient" temperature and there is no clearly defined range for "reducing" temperature within the "ambient" range. Thus, with respect to claims 49 and 53 and in the light of applicants' definitions, it is uncertain and indefinite what are the starting and final temperatures in the "reducing" step in the method for sterilization.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2, 3, 27, 28, 39-41, 50-52 and 81-88 are rejected under 35 U.S.C. 102(b) as being anticipated by Campalani et al. [U].

Claims are directed to a method for sterilizing heart valves that are sensitive to radiation wherein the method comprises step of applying to heart valves a stabilizing process and step of

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irradiating heart valves with a radiation at effective rate for a time effective to sterilize heart valves wherein the stabilizing process is reducing the temperature of heart valves to a level effective to protect heart valves from radiation and wherein radiation is gamma radiation. Some claims are/are further drawn to the stabilizing process and irradiation together being effective to protect from radiation. Some claims are further drawn to sterilizing the heart valves with biological contaminants and to the use of sensitizer in the method for sterilizing heart valves. Some claims are further drawn to temperature either less than ambient or below freezing point/glass transition point of the solvent surrounding the heart valves in the method for sterilizing heart valves. Some claims are further drawn to the recovery of the desired characteristics after sterilization greater than 50-100% of the pre-irradiated value in the method for sterilizing heart valves.

Campalani et al. teaches the aortic valve replacement with frozen gamma-irradiated homografts. In particular, the reference teaches a method for sterilizing heart valves or aortic valve homografts wherein the method comprises step of applying to heart valves a stabilizing process which is freezing to -70°C and step of irradiating the heart valves with gamma-irradiation with total dose 2.4 megarads or 24 kGy (page 559, col. 2, par. 2). The reference teaches storing of frozen 2 megarads gamma-irradiated heart valves for over a year before implantation and, thus, the radiation rate and time have been effective to sterilize the heart valves within the meaning of the claims 2 and 3. With respect to claims 50-52 and 81 the method for sterilization of the cited reference comprises irradiation at temperature below ambient which is below 0°C according to the applicants' definitions (specification page 27, last paragraph) and/or which is below freezing/glass transition point of a solvent which is either water in Hartmanns'

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solution or glycerol in the method of the cited reference. The reference teaches a recovery of some desired characteristics such as withstanding of the "tear out strength" test (page 559, col. 2, par. 2, last line) or survival of patients up to 16 years (fig. 2) and, thus, the recovery of desired characteristics is considered to be 50 -100% for at least some of the gamma-irradiated heart valves within the meaning of the claims 82-88. The collected homografts were subjected to sterilization and, thus, they are reasonably considered to be non-sterile and/or containing at least some amount of biological contaminants within the meaning of the claim 28. According to the applicants' definitions sensitizer is a substance that targets microbe to be sensitive to irradiation (specification page 17, last paragraph). Thus, in the method for sterilization of the cited reference the components of the Hartmans' solution are considered to be sensitizers within the meaning of the claim 27, for example: spore forming microbial contaminants/pathogens would be rendered sensitive to irradiation upon spore germination in the presence of aqueous solution with nutrients, for example; water, salts, lactate in the Hartmann's solution.

Thus, the method of the cited reference comprises all active steps and structural elements of the claimed method. Therefore, the reference by Campalani et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 2, 3, 6-14, 27, 28, 39-41, 49-53 and 81-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campalani et al. [U] taken with Dziedzic-Goclawska et al. [IDS reference, Paper No. 12].

Claims 2, 3, 27, 28, 39-41, 50-52 and 81-88 as explained above. Claims 6-15 are further drawn to ranges of radiation rate being less than 0.3 kGy/hour, no more than 3.0 kGy/hour, more than 3.0 kGy/hour or at least 45kGy/hour in the method for sterilizing heart valves. Claims 49 and 53 are further drawn to temperature being ambient/above ambient in the method for sterilizing heart valves.

The reference by Campalani et al. is relied upon as explained above for the disclosure of the method for sterilizing of frozen heart valves by gamma-irradiation. The cited reference by Campalani et al. teaches 2.4 megarads as total dose but it is silent with regard to irradiation rate. The cited reference by Campalani et al. teaches irradiation of frozen heart valves at but it lacks the disclosure related to irradiation of heart valves at "ambient" temperature or "above ambient".

The reference by Dziedzic-Goclawska et al. teaches that the effectiveness of the sterilization of tissue allografts or homografts including heart valves (page 261, par. 1) is considered with regard to and/or depends on the resistance of different microorganism contaminating the tissues of homografts or allografts. The reference teaches acceptable radiation ranges, including 17 kGy or up to 40-50 kGy, depending on biological contamination and on the tissue related considerations (see pages 277-280). The cited reference also suggests that the resistance of microorganisms to the sterilizing power of irradiation decreases at "elevated" temperature (page 277, par. 1).

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Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify radiation rate and/or time of exposure to radiation in order to achieve the required total dose of irradiation in the method disclosed by Campalani et al. with a reasonable expectation of success in sterilizing tissues homografts or allografts such as heart valves because the degree of radiation depends on a variable resistance of microbial contaminants/pathogens in the tissue allografts or homografts intended for reconstructive surgery {Dziedzic-Goclawska et al.}. One of skill in the art would have been motivated to adjust radiation rate and exposure time in order to achieve the required total radiation dose in order to prevent hazards of infectious disease transmission with tissues allografts including heart valves intended for reconstructive surgery as suggested by Dziedzic-Goclawska et al. The presently claimed method encompasses all possible radiation rate ranges from zero ("not more than 0.3", claim 9) and up to unlimited upper level ("at least 45", claim 14). It is considered to be within the purview of ordinary skill in the art to adjust radiation rate ranges and time of exposure to achieve the acceptable total radiation dose required for proper sterilization of tissue allografts. The required standards and recommended protocols for tissue sterilization by irradiation are established in the art of the tissue sterilization as adequately demonstrated by Campalani et al. and Dziedzic-Goclawska et al.

It would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to increase the temperature in the method for sterilization by irradiation in order to decrease the resistance of microbial contaminants in the tissue allografts as suggested by Dziedzic-Goclawska et al. for the expected benefit in preventing hazards of infectious disease

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transmission with tissues allografts including heart valves intended for reconstructive surgery as suggested by Dziedzic-Goclawska.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351.

The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

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September 5, 2003

VERA AFREMOVA

PATENT EXAMINER

V. Afremova